REMARKS

Claims 1-23 are pending in the present application with claims 17-21 withdrawn from further consideration. Claim 12 is objected to because of formalities. Claims 13-16 are rejected under 35 U.S.C §112, second paragraph. Claims 1-8 and 23 stand rejected under 35 U.S.C §103(a) as obvious in view of Fleming (USPN 6,503,409) and Coles (USPN 5,314,829). Claims 1-3 and 9-11 stand rejected under 35 U.S.C §103(a) as obvious in view of Fleming, Coles and Fritsch et al (US Publ. No. 2002/0058279). Claims 1, 12 and 22 stand rejected under 35 U.S.C §103(a) as obvious in view of Fleming, Coles and Storm et al (Nature Materials, 2003, 2, 537-540). Applicants acknowledge with appreciation that claims 13-16 would be allowable if rewritten in independent form including all the limitations of the base claim and any intervening claims. With this response, applicants amend claims #1, 12, 13, 17, 20, 22 and 23.

Claims 13-16, 22 and 23 are rejected under 35 U.S.C §112, second paragraph. Applicants amend claims 13, 22 and 23 to more particularly point out and distinctly claim the subject matter of the invention.

Applicants have rewritten claim 13 to be in independent form, including all the limitations of the base claim, in order to expedite prosecution.

Claims 1-8 and 23 stand rejected under 35 U.S.C §103(a) as obvious in view of Fleming (USPN 6,503,409) and Coles (USPN 5,314,829). Fleming discloses lithographic fabrication of nanoapertures. Fleming describes an aperture that is "nominally a rectangle (assuming that the trenches are perpendicular) having width equal to the width of the first trench 402 and length equal to the width of second trench 404" (4/46-49). Specifically, the aperture is designed so that "all three lateral dimensions characterizing the nanopore must be on the order of a few nanometers," if the aperture is to be useful for specified DNA sequencing applications (3/41-42).

To achieve these specified dimensions, Fleming uses a sequence of fabrication steps, the latter of which are depicted in Figures 3A and 3B. Fleming uses well-known fillet fabrication structures wherein:

> ...an out-of-plane structure with very small lateral dimensions is formed by defining the out-of-plane structure in a first material, growing or depositing a thin layer of a fillet material thereon, and removing excess

> material. The result is an out-of-plane fillet made of the fillet material where at least one dimension is roughly the thickness of said thin layer (3/58-65).

Specifically, a fillet structure is formed by creating a multi-layer material with 303 first oxide fillet embedded in silicon structural layer 302 (correspondingly 305 second oxide fillet embedded in silicon structural layer 304). A slice of the multi-layer material may be taken and rotated to an "out-of-plane" orientation (e.g. 90 degrees). In this first slice of the multi-layer material, the first oxide fillet 303 is embedded in the silicon structural layer 302 (Figure 3A). A second slice of the multi-layered material may also be taken, rotated "out-of-plane" and disposed in relation to the first slice, the second slice having second oxide fillet 305 embedded in the silicon structural layer 303 (Figure 3A).

> To form the aperture, it is sufficient to remove the oxide with a hydrofluoric acid etch. This yields the structure shown in FIG. 3B, where trenches 306 and 307 replace oxide fillets 303 and 305. The apertures appear at the point of the intersection of the two trenches, *and opens a passage between the two trenches whose size and shape is determined by the trenches* (4/28-34, emphasis added).

As a result of the disclosed fillet technique, the dimensions of the trench are defined by the thickness of the oxide fillet layer (303, 305).

In contrast, claim 1 recites:

> A process to fabricate nanopores and micropores, comprising the steps of:
>
> providing an integral <u>substrate member having a thickness and first and second opposing surfaces</u>;
>
> forming at least one <u>first V-shaped channel</u> lengthwise in a first direction <u>in said first surface</u>; and
>
> forming at least one <u>second V-shaped channel</u> lengthwise in a second direction <u>in said second surface</u>, said second direction being disposed at an angle relative to said first direction,
>
> wherein said first channel and said second channel extend inwardly from said first and second surfaces and intersect at a point, said point defining a pore extending through said substrate member from said first surface to said second surface; and
>
> wherein said pore extending through said substrate member from said first surface to said second surface is constructed to have dimensions suitable for transversely passing one or more biomolecules (emphasis added).

Specifically, claim 1 requires "an integral substrate member having a thickness and first and second opposing surfaces," forming a first V-shaped channel in said first surface, and forming a second V-shaped channel in said second surface.

The Examiner correctly notes that Fleming does not disclose "V-shaped channels and a plurality of V-shaped channels on the substrate" (Office Action of June 24, 2008, page 6). The Examiner looks to Coles to supply that which is missing from Fleming. However, the combination of references does not teach the claimed invention for two reasons: (1) Coles does not supply all of that which is missing from Fleming and (2) Fleming's fillet technique is incompatible with Cole's nano-machined grooves.

Firstly, Fleming does not teach or suggest "providing an integral substrate member having a thickness and first and second opposing surfaces" and forming first and second channels in the first and second surfaces, respectively, as recited in claim 1. Instead, Fleming explicitly discusses using two separate silicon structural layers, 302 and 304. Thus Fleming does not teach using an integral substrate member having first and second opposing surfaces. Each of Fleming's separate silicon structural layers 302, 304 have a trench running through the entire thickness of the layer, 303, 305, respectively, extending completely between opposing surfaces of the respective layer 203, 204. This is not the same as "forming at least one first V-shaped channel lengthwise in a first direction <u>in said first surface</u>" and "forming at least one second V-shaped channel lengthwise in a second direction <u>in said second surface</u>" of an integral substrate as required by claim 1.

Cole does not teach or suggest "providing a single substrate member having a thickness and first and second opposing surfaces" and forming first and second channels in the first and second surfaces, respectively, as recited in claim 1. Instead, Cole shows a "nano-machined groove" in a silicon substrate, the groove being "V-shaped, being about 50 nanometers in width at the top, the two sides thereof descending downwardly toward the apex at opposing 57 degree angles with respect to the vertical" (3/22-25). As evident in Figures 1 and 2, Cole's V-shaped grooves are formed on <u>only one surface</u> of the silicon substrate. "Grooves etched in a semiconductor surface are used to hold biological molecules such as individual DNA strands at

known reproducible locations. A grid of grooves is etched into <u>the surface</u> of a silicon substrate" (2/34-37). Because Cole does not teach or suggest forming a first groove in a first surface and a second groove in a second opposing surface of a single substrate, Cole does not supply that which is missing from Fleming.

Secondly, one of skill in the art would not combine Fleming's fillet technique with Cole's nano-machined grooves. Fleming's fillet technique uses the thickness of the oxide fillet layer (303, 305) to define the width of each trench. Fleming's method requires rotating each of the two fillet structures into an out-of-plane orientation, in order to attain the desired nanoscale aperture. By using this technique, Fleming achieves a nanoscale aperture using "well-known, controllable, and compatible microelectronic fabrication processes" (2/41-42). Cole's technique for creating grooves is entirely different. Formed directly into a single surface of a silicon substrate, the shape of Cole's V-shaped grooves have an angle that "is the result of the reactive ion etching process employed and the substrate material" (3/25-27). Cole uses nano-machining techniques to directly etch grooves in the major plane of the substrate. Whereas Fleming relies on a technique using an out-of-plane orientation to form trenches, Cole relies on a technique using an in-plane orientation to form grooves. Thus, contrary to the statement in the Office Action of June 24, 2008, it would <u>not</u> have been "prima facie obvious to one having ordinary skill in the art to modify the pore fabrication method of Fleming with the V-shaped channels on the surface of Coles with a reasonable expectation of success" (page 6).

Nor would one look to combine the teachings of Fleming with those of Cole, to achieve a pore "<u>wherein said pore extending through said substrate member from said first surface to said second surface is constructed to have dimensions suitable for transversely passing one or more biomolecules,</u>" as required by claim 1. Fleming admits the difficulty of achieving a suitable pore for DNA sequencing:

> A major problem to be overcome in the fabrication of nanopores for use in DNA sequencing is the miniscule size of the aperture required--nominally 2 nm or less in all dimensions. That is, all three lateral dimensions characterizing the nanopore must be on the order of a few nanometers (3/37-42).

While Fleming notes constraints on lateral dimensions of a characterizing nanopore, Fleming fails to note constraints on the width of the channel connecting to the pore. In Fleming, the

channel connecting to the pore is also of approximately 2-5 nm in thickness, an opening which is so narrow that it does not, in fact, promote DNA traversal. This channel width is highly undesirable since the DNA molecules or other biomolecules will be less likely to access the pore due to the large entropic barrier they have to overcome to reach the pore. While Fleming fails to teach a pore with "dimensions suitable for transversely passing one or more biomolecules," Cole does not teach or suggest anything resembling a structure suitable for transversely passing one or more biomolecules. In fact, Cole's grooves are specifically designed with dimensions intended to constrain DNA molecules and affix them in the grooves, "the strands are coaxed into the grooves preferably using gravity and pulsed electric fields which induce electric charge attraction to the molecular strands in the bottom surfaces of the grooves" (abstract). Constraining biomolecules and affixing them to a surface of a groove is not the same as transversely passing one or more biomolecules. Because Fleming does not disclose a pore with suitable dimensions for transversely passing biomolecules and Cole does not disclose structures for passing biomolecules at all, one would not look to Cole to remedy the deficits of Fleming.

Claims 1-3 and 9-11 stand rejected under 35 U.S.C §103(a) as obvious in view of Fleming, Coles and Fritsch et al. (US Publ. No. 2002/0058279). Fritsch does not supply that which is missing from Fleming and Coles, nor does Fritsch remedy the incompatibilities between Fleming's fillet techniques and Cole's nano-machined grooves.

Claims 1, 12 and 22 stand rejected under 35 U.S.C §103(a) as obvious in view of Fleming, Coles and Storm et al. (Nature Materials, 2003, 2, 537-540). Storm does not supply that which is missing from Fleming and Coles, nor does Storm remedy the incompatibilities between Fleming's fillet techniques and Cole's nano-machined grooves.

The fee for a two-month extension accompanies this response. If any additional fees are due, please charge our Deposit Account No. 08-0219, under Order No. 0012136.00131US1 from which the undersigned is authorized to draw.

Respectfully submitted,

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